

Serial No.: 09/782,386  
Filing Date: February 12, 2001

comprising a known sequence and a sugar and base free photoactivatable cross-linking agent, which when said probe sequence is hybridized to said target sequence, upon photoactivation forms a covalent bond between said probe sequence and said target sequence, said method comprising:

combining, in a hybridizing medium, a nucleic acid sample comprising said target and said probe under mild stringency hybridizing conditions for a time sufficient for said target and said probe to hybridize;

irradiating said hybridizing medium to form cross-links between said probe and target sequence to which said probe is hybridized to form cross-linked double-stranded nucleic acid;

separating nucleic acid in said hybridizing medium by denaturing electrophoresis and comparing the migratory rate of said cross-linked double-stranded nucleic acid to a known mismatched or matched cross-linked double-stranded nucleic acid standard, whereby the presence or absence of said at least one mismatch is determined.

- C1 cont
- 
5. (Amended) A method of detecting the presence or absence of at least one mismatch between a nucleic acid probe and a nucleic acid target, wherein said probe and target have sequences which differ by not more than five nucleotide base pair mismatches, said target sequence comprises a nucleic acid molecule of from about 25 to 300 nt and said probe comprising a known polynucleotide sequence of from 15 to 50 nt and a sugar and base free photoactivatable cross-linking agent, which when said probe sequence is hybridized to said target sequence, upon photoactivation forms a
- C2

Serial No.: 09/782,386  
Filing Date: February 12, 2001

covalent bond between said probe sequence and said target sequence, said method comprising:

combining, in a hybridizing medium, a nucleic acid sample comprising said target and said probe under mild stringency hybridizing conditions for a time sufficient for said target and said probe to hybridize;

irradiating at a wavelength in the range of about 300-400 nm said hybridizing medium to form cross-links between said probe and target sequence to which said probe is hybridized to cross-linked double-stranded nucleic acid;

separating nucleic acid in said hybridizing medium by denaturing electrophoresis and comparing the migratory rate of said cross-linked double-stranded nucleic acid to a known mismatched or matched cross-linked double-stranded nucleic acid standard, whereby the presence or absence of said at least one mismatch is determined.

---

10. (Amended) A method of detecting the presence or absence of at least one mismatch between a nucleic acid probe and a nucleic acid target, wherein said probe and target have sequences which differ by not more than five mismatches, said target sequence comprising a nucleic acid molecule of from about 25 to 300 nt and wherein said probe comprises a known polynucleotide sequence of from 15 to 50 nt and a sugar and base free photoactivatable cross-linking agent, which when said probe sequence is hybridized to said target sequence, upon photoactivation forms a covalent bond between said probe sequence and said target sequence, said method comprising:

Serial No.: 09/782,386  
Filing Date: February 12, 2001

combining, in a hybridizing medium, a nucleic acid sample comprising said target and said probe under mild stringency hybridizing conditions equivalent to a temperature in the range of 25 -70°C and with 0.1 -1.5 M sodium for a time sufficient for said target and said probe to hybridize;

irradiating at a wavelength in the range of about 300-400 nm said hybridizing medium to form cross-links between said probe and target sequence to which said probe is hybridized to form cross-linked double-stranded nucleic acid;

separating nucleic acid in said hybridizing medium by denaturing gel electrophoresis and comparing the migratory rate of said cross-linked double-stranded nucleic acid to a known mismatched or matched cross-linked double-stranded nucleic acid standard, whereby the presence or absence of said at least one mismatch is determined.

C3' cont

---

#### REMARKS

Claims 1-11 are pending, and stand rejected. Claims 1, 5, and 10 have been amended. Support for the amendments can be found at p.9, lines 25-33 of the specification. A marked-up version of the changes made to the claims is attached hereto as Appendix B. The attached page is captioned, "Version with markings to show changes made." Appendix A is a copy of the current claims has been attached for the Examiner's convenience. Favorable consideration of the following comments relative to the outstanding rejections as they may apply to the present claims is respectfully requested for the following reasons.